REMARKS

With the entry of the present Amendment, claims 47-58 are in this application. Claims 1-46 have been canceled without prejudice. The recitation of a nucleic acid **extracted, purified or amplified from the sample** is supported by the as-filed application. *See* page 21, lines 13-15; page 24, lines 4-10; page 22, lines 1-7 and Examples 8 and 12. The language of new claim 56 is supported by the context of the Specification. None of the amended claims provided herein constitutes the addition of new matter.

The following comments, responsive to the final Office Action, are provided.

The Rejections under 35 U.S.C. 112, second paragraph

Claims 1, 5-11 and 13-15 had been rejected under 35 U.S.C. 112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter Applicants regard as the invention. Applicants respectfully traverse this rejection.

In Item 23 of the final Office Action, the Examiner had indicated that recitation of "consecutive" nucleotides of nucleotides 1147-1740 of SEQ ID NO:1 would resolve the issue of alleged indefiniteness.

In the interest of advancing prosecution and without acquiescing to the rejection, new claim 47 recites a sequence of 15 or more **consecutive** nucleotides, in accordance with the Examiner's suggestion. Withdrawal of this rejection is now respectfully requested.

The Rejections under 35 U.S.C. 102

Claims 1, 5-9, 13-15 and 46 had been rejected under 35 U.S.C. 102(b) as allegedly anticipated by Gardner *et al.* (1993, Nucleic Acids Research). Applicants respectfully traverse this rejection.

In the interest of advancing prosecution and without acquiescing to this rejection, new claim 47, which replaces claim 1, specifies the particular sequence of the probe or primer used in the detection methods, namely, at least 15 consecutive nucleotides of nucleotides 1147-1740 of SEQ ID NO:1 or at least 15 consecutive nucleotides of a sequence complementary to nucleotides 1147-1740 of SEQ ID NO:1. The recitation of the noted portion of SEQ ID NO:1 was in concert with the suggestion of the Examiner in a previous Office Action.

Moreover, the Gardner reference makes no teaching of a method for detecting *Plasmodium* organisms which infect humans in biological samples by hybridization or by polymerase chain reaction using probes or primers as specified above. The Gardner reference discusses the relatedness of certain sequences across a variety of organisms, including yeast, bacteria, filamentous fungi, algae and plants. In fact, Table 1 on page 1070 of the cited 1993 Gardner reference includes 44 segments of segments of plasmodium sequence, which were conserved in comparison to *E. coli* sequences. The Gardner (1993) reference does not show the use of the particular sequence (nucleotides 1147-1740 or a 15 consecutive-nucleotide probe or primer derived in sequence therefrom) in detection methods. An important aspect of the present invention is the recognition that nucleotides 1147-1740 of SEQ ID NO:1 are highly conserved among Plasmodia that infect humans, such that a primer or probe of at least 15 consecutive nucleotides of this sequence hybridize to the corresponding sequences within the extrachromosomal genetic elements of the human *Plasmodium* pathogens.

With respect to arguments previously provided, it appears that the Examiner has not noted that arguments related to teachings of the sequence of the probe or primer were in respect of the rejection, now withdrawn, over the Gardner (1994) reference.

In view of the foregoing discussion and the claims presented herein, Applicants respectfully maintain that the invention as claimed is not anticipated by the cited Gardner reference, and withdrawal of the rejection is requested.

The Rejection under 35 U.S.C. 103(a)

Claims 14-15 had been rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Gardner *et al.* (1993) in view of Obst *et al.* (1990). Applicants respectfully traverse this rejection.

The cited Gardner reference is said to teach a method of detecting a human plasmodium malarial agent in a biological sample, by contacting a blood-derived (erythrocyte) sample with a probe or primer that comprises a LSU rRNA nucleic acid sequence of SEQ ID NO:1, nucleotides 1147-1740 that is conserved and found in an extra chromosomal element.

Applicants have discussed the Gardner (1993) reference above. This reference relates to an analysis of sequence relatedness across a wide variety of organisms, and there is no teaching or suggestion of SEQ ID NO:1, nucleotides 1147-1740, or other plasmodium sequence, as useful in methods for detection of plasmodial species which infect humans in biological samples. There appears to be no discussion of the sequence relatedness for the noted sequence among different species of Plasmodium which are pathogenic to humans.

The Obst *et al.* reference relates to mapping sequences on plant chromosomes and to localizing nuclear sequences in *Plasmodium berghei* cells in blood smears. Unique nuclear sequences and rRNA probes were used in the experiments described. There is no indication in this reference that the use of probes or primers of the sequences encompassed by that recited in claim 1 would be useful in methods for detection of a Plasmodium in a biological sample, and there is no discussion of the conservation of the recited sequence among Plasmodium species. At most, this reference would provide an invitation to experiment, but there is no teaching or suggestion of the specifically claimed methods nor is there any provision of any reasonable probability of success in the claimed methods.

Applicants respectfully submit that there is no motivation provided in the cited references for their combination. The cited 1993 Gardner reference discusses phylogenetic relationships based on a subset of rRNA sequences. The cited Obst reference shows hybridization of a relatively large probe to a slide of *Plasmodium berghei*, but provides no teaching as to the sequence relatedness for other species of Plasmodium which are human pathogens. The context appears to be detection of particular sequences but not carrying out a sensitive and reliable method to detect the organism *per se.*

In the absence of the cited references providing a reasonable probability of success, as required by In re O'Farrell, 7 U.S.P.Q.2d 1673 C.A.F.C, 1988, Applicants respectfully state that the invention as claimed is not *prima facie* obvious over the cited references, and the rejection should be withdrawn.

Conclusion

This Amendment is accompanied by a Request for Continued Examination, a Petition for Extension of Time and a check in the amount of $ 1,125.00 ($385.00 for the Request for Continued Examination and $740.00 for the extension of time). It is believed that the present submission does not require the payment of any additional fees under 37 C.F.R. 1.16-1.17. If the amount submitted is incorrect, please charge any deficiency or credit any overpayment of fees due under the foregoing Rules to Deposit Account No. 07-1969.

Respectfully submitted,

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